in co-culture with rat cardiomyocytes. Spontaneous beating of ASCs was most pronounced when there was cell-cell contact with rat CMCs. While all of the non-red cells with typical rat CMC morphology stained positive for cardiac-specific alpha-actinin, few fluorescent ASCs were also positive for cardiac-specific alpha-actinin.
Conclusions: Our experiments suggest that human subcutaneous adipose tissue contains cells which in culture express the stem cell marker CD34 and have potential to acquire a cardiomyocyte phenotype. Considering that large quantities of fat can be easily harvested from patients, cell therapy using autologous ASCs for cardiac regeneration or repair may represent a novel therapeutic option for patients with cardiomyopathy.

1068-127 Ischemic Precondition Improves Performance of the Hearts With Coronary Delivery of Embryonic Stem Cells: Assessment by a Langendorff Perfusion Model

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Background: Intracoronary stem cell perfusion is a novel therapy for heart failure. However, concern has been raised about the biosafety of this therapy. This study aimed at analyzing functional and metabolic alterations in the hearts perfused with embryonic stem cells (ESCs).
Methods: Hearts of C57BL/6J mice were perfused with modified Krebs-Henseleit buffer on a Langendorff device. Ischemia-preconditioning (IPC) was performed. Thereafter, fluorochrome tagged murine D3 ESCs were transfused and hemodynamic parameters, e.g., coronary flow (CF), heart rate (HR), left ventricular peak pressure (LVP), +dp/dtmax, and -dp/dtmax, were recorded. Coronary effluents were collected to determine cardiac troponin I (cTnI). After perfusion, the hearts were fixed and subjected to histopathological studies.
Results: Murine hearts with coronary ESC perfusion at 10^6 cells/ml/min or less showed no major changes in contractility and rhythm. However, with cell concentration increase ($2.5 \sim 5 \times 10^6$ cells/ml/min), the hearts were dysfunctional, with declines in all hemodynamic parameters and marked increase in cTnI in coronary effluents. Interestingly, IPC significantly reduced the adverse impact of high ESC perfusion by nearly 50% compared to heart perfusion without IPC. Improved morphology occurred in IPC myocardium with ESC perfusion.
Conclusions: Perfusion of ESC at high concentrations may cause cardiac dysfunctions. IPC may increase tolerance to stem cell perfusion and improve performance of the hearts.

Table 1. Hemodynamic and Biochemical Alterations at 30 minute after Stem Cells Perfusion

	ESC Perfusion without IPC *(X 10^6 cells/ml/min)*				**ESC Perfusion with IPC** *(X 10^6 cells/ml/min)*
	0	*1.0*	*2.5*	*5.0*	*5.0*
CF	-10.8 ± 7.2%	-22.2 ± 28.0%	-55.0 ± 32.2%	-63.6 ± 29.7%	-31.4 ± 16.7%
HR	-10.2 ± 11.8%	-22.4 ± 24.5%	-19.4 ± 23.7%	-49.7 ± 22.0%	-24.9 ± 10.3%
LVP	-1.9 ± 20.7%	-7.0 ± 19.1%	-30.7 ± 24.5%	-50.2 ± 39.0%	-24.4 ± 32.9%
+dp/dt	+2.6 ± 15.7%	-7.6 ± 41.3%	-40.4 ± 27.0%	-57.6 ± 36.3%	-32.8 ± 25.1%
-dp/dt	-12.8 ± 22.3%	-26.0 ± 24.8%	-50.9 ± 23.5%	-69.1 ± 29.8%	-45.2 ± 20.8%
cTnI	+20.9 ± 67.7%	+42.6 ± 70.8%	+256.6 ± 93.1	+1403.4 ± 849.9%	+6.9 ± 20.5%

1068-128 Ranolazine Inhibits Late Sodium Current in Isolated Left Ventricular Myocytes of Dogs With Heart Failure

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Background: We recently reported the existence of novel, ultraslow late sodium current (I_{NaL}) in left ventricular (LV) myocytes isolated from failing human and dog hearts. Augmented I_{NaL} has been implicated in ventricular repolarization abnormalities in chronic heart failure (HF). In the present study we sought to determine the effects of ranolazine (RAN), a novel anti-ischemic drug, on peak (I_{NaT}) and late I_{NaL}, action potential (AP) duration (APD), and early afterdepolarizations (EAD's) in LV myocytes isolated from dogs with chronic HF.
Methods: Experiments were carried out in mid-myocardial LV myocytes isolated from the hearts of 6 dogs with chronic HF produced by the intracoronary microembolization. AP's were recorded using the β-escin perforated patch method at a frequency of 0.5 Hz and 35°C. Both I_{NaT} and I_{NaL} were recorded by a conventional whole-cell patch-clamp technique. Amplitude and decay of I_{NaL} were measured at 200 ms after the onset of a 2 second-long depolarization to -30 mV at 0.1 Hz.
Results: RAN, at a concentration of 5 μmol/L, reversibly shortened the APD from a baseline value of 556 ± 53 ms to 316 ± 34 ms (mean ± SEM, n=8 cells, P<0.05). RAN also decreased APD dispersion and suppressed EADs. At the same concentration (5 μmol/L), RAN shifted the mid-point steady-state availability of I_{NaL} by -7.7±1.2 mV (n=5 cells). The potency (IC_{50} value) of RAN to cause resting block of I_{NaL}, assessed by a single-site binding model, was 6.7 μM (n=6 cells). In contrast, 5μmol/L of RAN did not significantly inhibit I_{NaT}. The IC_{50} for inhibition by RAN of I_{NaT} was 244 μmol/L (n=14 cells). RAN did not affect the decay time course of I_{NaL}.
Conclusion: In these experimental conditions, RAN is approximately a 36-fold more potent blocker of late I_{Na} than peak I_{Na}, and reverses the ventricular repolarization abnormalities (APD prolongation and EADs) of failing myocytes. These findings suggest that ranolazine, by inhibiting I_{NaL}, may suppress ventricular arrhythmic activity associated with augmented I_{NaL} during repolarization of the action potential in HF.

POSTER SESSION

1069 Heart Failure: Outcomes I

Monday, March 08, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1069-105 50-Year Heart Failure Mortality for England and Wales

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Aim: To analyse heart failure mortality trends for England and Wales over fifty years, from 1951 to 2000.
Design: A retrospective observational study using death certificate and population data from the Office for National Statistics for England and Wales.
Results: Unadjusted heart failure deaths rose by 3.3 from approximately 3400 in 1951 to 11400 in 1974. Since then, heart failure deaths have fallen by approximately 25% to 8600 in 2000. Throughout this period, the number of people in the Western world surviving beyond 70 years has steadily increased and so it would be expected that the number of heart failure deaths would increase too. However, even when heart failure mortality is standardised to allow for changes in the age, sex and size of the population, there was approximately a 2.2 rise in mortality from 1951 to the mid-70's and since then, there has been a substantial and sustained decline in mortality of approximately 55% by 2000. The unadjusted female heart failure death rate has been between 1.5 and 2 times that of males since the early 70's. However, this higher mortality rate is much less marked when the differences between the age distribution and sizes of the male and female populations are taken into account. When compared with trends in mortality for coronary artery disease the changes with time and by age group are remarkably similar.
Conclusion: The trends in heart failure mortality for England and Wales over 50 years may reflect genuine changes in disease incidence, influenced by current changes in lifestyle and the medical management of cardiac disease. These changes are similar to those seen in coronary artery disease. The data available cannot estimate the absolute incidence of deaths involving heart failure because of death certificate completion and the trends in heart failure diagnosis over time.

1069-106 Deaths From Heart Failure in the Era of the Implantable Defibrillator

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Background: Despite the growing number of indications for implantable cardioverter-defibrillators (ICD) and the improving survival with heart failure (HF), morbidity and mortality from progressive HF remain substantial.
Methods: To determine the prevalence of ICDs in patients dying with advanced symptomatic HF, we reviewed all of the patients followed in the HF program with an ejection fraction (EF) less than or equal to 35% and recent NYHA class III/IV symptoms who died in the hospital or after discharge with hospice between 1/1/00 and 9/1/03.
Results: There were total of 126 deaths, of which 68 (54%) met the criteria for entry into the study (57 patients died in the hospital, 9 patients died in hospice). Patients had HF for a mean of 5.8 years, had a mean age of 61 years, and 75% were men. The mean EF was 19% and moderate to severe right ventricular dysfunction was present in 62%. Beta-blockers and/or amiodarone were taken by 75% of patients. Ischemic cardiomyopathies (CM) accounted for 55% of patients, of whom 79% had prior bypass. The mean of the worst laboratory values in the last six months of life include a sodium of 127, blood urea nitrogen of 97 and creatinine of 3.7.
Of the 68 deaths, 34 (50%) had an ICD, three of whom also had biventricular pacing. The prevalence of ICDs was 47% in patients with ischemic CM and 53% in patients with nonischemic CM. Advance directives specified limits on resuscitation in 24 (71%), of which 13 (54%) had defibrillation inactivated (10/22 in hospital, 3/3 in hospice), but only a median of 1 day prior to death. Overall, the ICDs were implanted a median of 21.5 months (range 1-144) prior to death, but 11 (32%) were implanted less than 1 year before death and 6 (18%) less than 6 months before death (5/6 of these were implanted for primary prevention).
Conclusions: In patients with advanced HF, there is a high prevalence of ICDs, regardless of the etiology of HF. However, the benefit from preventing sudden death may be diminished as the likelihood of terminal hemodynamic deterioration increases. Therefore, management of ICDs will become an increasingly important aspect of care at the end of life.